IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., et al., Defendants.	Case No. 1:18-cv-01043-LPS [redacted] REDACTED PUBLIC VERSION

DEFENDANTS' OPPOSITION TO NOVARTIS'S
MOTION FOR PRELIMINARY INJUNCTION

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PATENTS

U.S. Patent No. 9,187,405 ..... '405 patent

MISCELLANEOUS

PTAB Final Written Decision in IPR2017-00854
Trenchard Ex. 73 (D.I. 365) ..... FWD

Abbreviated New Drug Application ..... ANDA

Clinical Trial entitled "**F**ingolimod **R**esearch **E**valuating **E**ffects of
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Kappos et al., *Design of A Randomised, Placebo-Controlled Study of Oral Fingolimod (FTY720) In Relapsing-Remitting Multiple Sclerosis*, 253(Supp. 2) J. NEUROLOGY II/143 (Abstract P569)

(2006) ..... Kappos 2006

Opening Brief in Support of Novartis's Motion for A Preliminary Injunction (D.I. 358) ..... Br.

New Drug Application ..... NDA

Novartis Pharmaceuticals Corp. (Plaintiff) ..... Novartis

Secondary Progressive Multiple Sclerosis ..... SPMS

Relapsing Remitting Multiple Sclerosis ..... RRMS

U.S. Food and Drug Administration ..... FDA

U.S. Patent and Trademark Office ..... PTO

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INTRODUCTION

Novartis moved for a preliminary injunction to keep competing products off the market. Yet, to obtain such extraordinary relief, Novartis must clearly show that it will likely succeed in proving the patent-in-suit valid and that it will suffer substantial and immediate irreparable harm absent an injunction. Novartis cannot make either showing. More than a year before the named inventors applied for the patent-in-suit, U.S. Patent No. 9,187,405 ("'405 patent"), the details of Novartis's Phase III clinical trial for fingolimod, claimed in the '405 patent, were published. The published disclosure was robust – even more robust than the patent itself – but was never submitted to the Patent Office during either prosecution or the Apotex IPR. Novartis's publication disclosed each and every limitation of the asserted claims; if this prior art does not anticipate, the '405 patent is invalid for lack of written description and utility under Section 112 of the Patent Act. Novartis's preliminary injunction quest therefore falls well short of establishing likelihood of success on the merits.

Novartis faces another high hurdle in trying to establish that generic competition would cause it irreparable harm: its own inaction. Years ago, Novartis submitted the patent-in-suit for listing in FDA's Orange Book as covering Gilenya. Novartis then received several paragraph IV notice letters informing Novartis of the ANDA filers' intent to market their generic products before the '405 patent's expiration and immediately upon receiving FDA approval. But Novartis did not sue under the Hatch-Waxman Act. Having now delayed until the eleventh hour to bring this action,[1] Novartis cannot establish that its various self-inflicted "potential injuries" constitute irreparable harm. Even more, Novartis's irreparable harm arguments fail because at their core, Novartis's alleged harms are monetary ones that can be easily calculated.

[1] Novartis litigated its earliest-expiring patent, U.S. Patent No. 5,604,229 ("'229 patent") through appeal, with its formulation patent (U.S. Patent No. 8,324,283) invalidated at the Patent Office. Novartis uses the pending loss of protection of the '229 patent as its basis for urgency here.

NATURE AND STAGE OF THE PROCEEDINGS

This action was filed on July 16, 2018, against nearly two dozen defendants. Many fewer active defendants remain. Novartis alleges that the defendants infringed claims 1-6 of the '405 patent by submitting ANDAs seeking approval for fingolimod 0.5 mg capsules, which, if approved, would be generic alternatives to Novartis's Gilenya®. The parties have conducted significant discovery: the deadline for substantial completion of document production was January 15, 2019, and fact discovery closes June 4, 2019. The parties are currently briefing claim construction, and the *Markman* hearing is set for April 23, 2019. The hearing on Novartis's motion for preliminary injunction will be held on June 21, 2019, and trial is set for March 2-6, 2020. The FDA has tentatively approved the ANDAs for several of the Defendants. Final approval of any Defendant's ANDA is not expected until at least August 18, 2019, upon the expiration of the pediatric exclusivity for the '229 patent.

Novartis moved for a preliminary injunction on February 19, 2019. Defendants' opposition is supported by evidence already of record in the proceedings, and declarations from Dr. Paul Hoffman, M.D., a treating neurologist and clinical researcher in the field of MS, and Mr. Ivan Hofmann, Vice President and Managing Director at Gleason IP, an expert economist who has been qualified by this Court and others on the issues of damages, irreparable harm, and commercial success in pharmaceutical patent litigation. Defendants also submit the declaration of Bryan Beel, Ph.D., and accompanying exhibits thereto.

SUMMARY OF ARGUMENT

Novartis is not entitled to a preliminary injunction because its inconsistent arguments individually and collectively fail as a matter of law:

1. *Novartis's Invalid Patent.* Novartis cannot show it will likely succeed on the merits because there is a substantial question as to validity, at least because the '405 patent is

invalid for anticipation. More than a year before the earliest effective filing date, Novartis published a method of treating relapsing-remitting multiple sclerosis in more detail than it ever provided in the '405 patent's specification and claims. If the prior art's complete disclosure of the claimed invention does not anticipate the asserted claims, then those claims must fail for lack of written description and/or lack of enablement and utility.

2. *Novartis's Alleged "Irreparable" Harm.* Novartis must show that it will suffer substantial and immediate irreparable injury absent an injunction. Novartis alleges dire outcomes if Defendants are not enjoined from launching, but none of these purported injuries is irreparable, let alone the type of harm recognized as requiring injunctive relief. Novartis has long planned for generic entry of fingolimod, including through market activities and [redacted] When generic entry eventually occurs, Novartis will sustain no harm that could not be remedied by monetary damages, if necessary.

STATEMENT OF FACTS

I. THE PATENT-IN-SUIT (U.S. PATENT NO. 9,187,405).

Novartis listed four patents in FDA's Orange Book for Gilenya® 0.5 mg capsules. Exclusivity for the '229 patent ends August 18, 2019. One patent expired; another was held invalid. Only the '405 patent remains, with pediatric exclusivity until December 25, 2027. Ex. 1.

The '405 patent is directed to the use of sphingosine 1-phosphate (S1P) receptor agonists for the treatment of demyelinating diseases such as multiple sclerosis. '405 patent at 1:5-8; P. Hoffman ¶ 73. The specification describes a genus of sphingosine analogs ('405 patent at 1:15-18), including 2-amino-2-[2-(4-octylphenyl)ethyl]propane-l,3-diol hydrochloride, also

known as fingolimod hydrochloride or FTY720.[2] '405 patent at 8:18-30; P. Hoffman ¶ 73.

Novartis asserts infringement of all claims of the '405 patent (claims 1-6). Independent claims 1, 3, and 5 each claim a method of using fingolimod, or a pharmaceutically acceptable salt form, to treat patients suffering from relapsing-remitting multiple sclerosis ("RRMS"). *See* '405 patent at 12:49-55, 59-64, 13:1-6. Each method claimed in the '405 patent includes only the single step of orally administering 0.5 mg of fingolimod or its salt to a person with RRMS. *See id.* Claim 1 recites:

> 1. A method for **reducing or preventing or alleviating relapses in** [RRMS] in a subject in need thereof, comprising *orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.*

Id. at 12:49-55 (emphases added). Claims 3 and 5 differ from claim 1 only in their preambles (claim 3: "A method for **treating** [RRMS] in a subject in need thereof"; claim 5: "A method for **slowing progression** of [RRMS] in a subject in need thereof.) *Id.* at 12:59-64; 13:1-6 (emphases added). Claims 2, 4, and 6 limit the methods of claims 1, 3, and 5, respectively, to using fingolimod hydrochloride. *See, e.g., id.* at 12:56-58.

II. KAPPOS 2006 AND NOVARTIS'S FINGOLIMOD CLINICAL TRIALS RENDER THE PATENT INVALID.

In 2006, Novartis broadly and repeatedly published the details of its fingolimod Phase III trial, revealing to the public the method it claimed more than a year later in the '405 patent. By then, fingolimod (and FTY720, its hydrochloride salt) had long been known in the art. Large-scale clinical trials were completed, which demonstrated that fingolimod could treat patients suffering from RRMS, and further trials were ongoing. Novartis publicized the results of the

[2] The prior art makes clear that "FTY720" was known to refer to 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride, or fingolimod hydrochloride, as recited in the claims of the '405 patent. *See* P. Hoffman ¶¶ 55, 77; Steinman ¶ 38.

Phase II clinical trials and initiated a Phase III clinical trial called FREEDOMS, for **F**ingolimod **R**esearch **E**valuating **E**ffects of **D**aily **O**ral therapy in **M**ultiple **S**clerosis, which was described extensively in prior art not submitted to the PTO during prosecution of the '405 patent application. Ex. 1; Trenchard Ex. 5 (Kappos 2005) at NPCFINGO006023997; Trenchard Ex. 34 (Chavez) at NPCFINGO006028252-54; Trenchard Ex. 69 (Novartis Press Release) at NPCFINGO006028800-01; Trenchard Ex. 79 (Novartis Form 6-K) at DEFSPRIORART-000345-46; *see also* Trenchard Ex. 7 (File History U.S. Patent Application No. 14/257,342) at NPCFINGO006024707-855.

In fact, in Kappos 2006,[3] Novartis published information presented at the Sixteenth Meeting of the European Neurological Society, including the results of a Phase II clinical study administering fingolimod to patients with RRMS. *Id.* at DEFSPRIORART-000172.[4] Kappos 2006 disclosed that the results of the Phase II study indicated that treatment with fingolimod reduced inflammatory activity on MRI by up to 80% and relapse rates by more than 50% compared to placebo. *Id.*

Kappos 2006 also disclosed the ongoing Phase III study, the FREEDOMS study, that included approximately 1,100 patients from more than 100 centers worldwide who were randomized in a 1:1:1 ratio to once-daily fingolimod 1.25 mg, fingolimod 0.5 mg, or placebo, for

[3] Kappos 2006 is an abstract published in the Journal of Neurology in May 2006, received by the British Library no later than June 9, 2006, and indexed no later than June 22, 2006, and therefore qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Ex. 2 at DEFSPRIORART-000168 (showing dates).

[4] The first priority document for the '405 patent is a British patent application filed on June 27, 2006. For purposes of pre-AIA 35 U.S.C. § 102(b), the relevant date is that of the first United States filing. *See* 35 U.S.C. § 119(a) (pre-AIA); MPEP § 706.02. In this case, "the actual filing of the application in this country" is no earlier than June 25, 2007, the filing date of PCT/EP2007/005597. Therefore, publications that pre-date June 25, 2006, are prior art to the claims of the '405 patent under 35 U.S.C. § 102(b). *See* MPEP § 2123(II); *In re Katz*, 687 F.2d 450, 454 (CCPA 1982).

up to 24 months. *Id*. at DEFSPRIORART-000173; P. Hoffman ¶ 68. FREEDOMS considered outcome measures including relapse rate and disability progression, and assessed relapse severity, quality of life, and safety. *Id*. Kappos 2006 reported that FREEDOMS would help define the role of fingolimod as a new oral treatment option for RRMS. *Id*. at DEFSPRIORART-000173; P. Hoffman ¶ 70.

A person of ordinary skill in the art ("POSA") understood Kappos 2006 to indicate that the regimen necessarily excludes a loading dose. P. Hoffman ¶¶ 80-82. Notably, Kappos 2006 was never disclosed to, or considered by, the PTO during prosecution or IPR.

III. DEFENDANTS' NOTICE LETTERS AND PRIOR LITIGATION.

Defendants submitted ANDAs with patent certifications to other patents before the '405 patent was listed in FDA's Orange Book. After receiving Defendants' Notice Letters, Novartis brought suit only on the '229 patent. Therefore, despite notice and opportunity, Novartis did not assert the '405 patent until years later.

In February 2017, Apotex[5] petitioned for *inter partes* review, contending the '405 patent was obvious ("Apotex IPR"); the PTAB ruled in Novartis's favor on July 11, 2018. FWD. Novartis filed this action five days later, belatedly asserting the patent on which it had elected not to sue for over two years.

The primary grounds asserted in the Apotex IPR were, unlike here, based on obviousness. The only asserted anticipation ground in the IPR relied on a reference referred to as Kappos 2010, which is not at issue here, and an attack on the '405 patent's priority date, which is not necessary here. *See* FWD at 8, 40-45. That challenge required Apotex to establish that Kappos 2010 was prior art to the '405 patent even though the reference was filed after the '405 patent's earliest application date. Apotex argued that the claim limitation "absent an immediately

[5] Apotex has since settled with Novartis and is not a party to the present case.

preceding loading dose regimen" was new matter, not entitled to the original filing date, because the phrase first appeared in a 2014 amendment to the application. *Id.* at 40 (citations omitted). Therefore, according to Apotex, the claims were only entitled to a 2014 priority date, making Kappos 2010 prior art.

At Novartis's urging, the PTAB found the "absent an immediately preceding loading dose" limitation supported by the '405 patent specification as originally filed. *Id.* at 44-45. In support of Novartis's position, the same Dr. Jusko opining here pointed to the Clinical Trial section in column 11 of the '405 patent specification, and testified that a POSA did not need an express recitation of the "no loading dose" instruction to understand that a loading dose was not included. Trenchard Ex. 28 (Jusko Second Decl.) at ¶¶ 174-75. Another current Novartis expert, Dr. Steinman, offered similar testimony. Trenchard Ex. 27 (Steinman Decl.) at ¶¶ 10, 182–87.

NOVARTIS IS NOT ENTITLED TO A PRELIMINARY INJUNCTION

"[A] preliminary injunction is a drastic and extraordinary remedy that is not to be routinely granted." *Intel Corp. v. ULSI Sys. Tech., Inc.*, 995 F.2d 1566, 1568 (Fed. Cir. 1993); *see also Sebela Int'l Ltd. v. Actavis Labs. FL, Inc.*, No. 17-4789-CCC-MF, 2017 WL 4782807, at *2 (D.N.J. Oct. 20, 2017) ("Accordingly, the party seeking a preliminary injunction bears the burden of establishing its entitlement to such extraordinary relief."). A "plaintiff seeking a preliminary injunction must establish that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest." *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008); *Apple, Inc. v. Samsung Elecs. Co.*, 678 F.3d 1314, 1323 (Fed. Cir. 2012). "[A] movant must establish the existence of both of the first two factors to be entitled to a preliminary injunction." *Altana Pharma AG v. Teva Pharm. USA, Inc.*, 566 F.3d 999, 1005 (Fed. Cir. 2009); *Noven Pharm., Inc. v. Mylan Techs. Inc.*, No. 17–1777-LPS, 2018 WL 4052418, at

*2 (D. Del. Aug. 20, 2018) (citing *Altana*, 566 F.3d at 1005). Thus, if Novartis fails to carry its burden on either of the first two elements, this Court's inquiry is at an end and no injunction may issue. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 572 U.S. 1301 (2014) (Roberts, C.J., in chambers) (holding that the availability of patent infringement damages precludes injunctive relief and refusing "the extraordinary relief" of enjoining generic entry).

"An accused infringer can defeat a showing of likelihood of success on the merits by demonstrating a substantial question of validity or infringement." *Trebro Mfg., Inc. v. FireFly Equip., LLC*, 748 F.3d 1159, 1165 (Fed. Cir. 2014). Therefore, "[i]f the alleged infringer raises a 'substantial question' regarding invalidity, i.e., asserts an invalidity defense that the patentee cannot prove 'lacks substantial merit,' the preliminary injunction should not issue." *Entegris, Inc. v. Pall Corp.*, 490 F.3d 1340, 1351 (Fed. Cir. 2007) (quoting *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1364 (Fed. Cir. 1997)).

I. NOVARTIS CANNOT SHOW IT IS LIKELY TO SUCCEED ON THE MERITS BECAUSE OF SUBSTANTIAL QUESTIONS CONCERNING THE VALIDITY OF THE '405 PATENT

There are substantial questions regarding the validity of the '405 patent under at least two theories—anticipation by the prior art under 35 U.S.C. § 102 or failure to meet one or more of the requirements of 35 U.S.C. § 112 and/or § 101. These defenses are matters of law, either of which suffices to render the patent invalid. Because the evidence shows at least a substantial question as to validity on one or more grounds, Novartis is not entitled to injunctive relief. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1358 (Fed. Cir. 2001) (holding that a defendant need only raise a substantial question concerning validity to defeat a preliminary injunction); *see also Noven*, 2018 WL 4052418, at *2.

A. All Claims of the '405 Patent Were Anticipated by the Prior Art.

1. Level of Ordinary Skill in the Art

A POSA with respect to the claimed subject matter would be a person with a M.D. having a specialty in neurology who has several years of experience treating multiple sclerosis patients in a clinical setting.[6] P. Hoffman ¶ 32. In view of the relatively high level of skill and the clear teachings in the prior art, the level of skill of the POSA is not dispositive of any invalidity issue.

2. The Apotex IPR

As described above, in the Apotex IPR, Novartis and its current experts argued that a POSA did not need to see an express recitation of the "no loading dose" instruction to understand that a loading dose was not included in a method of treating RRMS. Novartis successfully persuaded the PTAB to adopt that position, and prevailed in the IPR. Thus, by its statements in the '405 patent's intrinsic record,[7] Novartis is foreclosed from now advocating for any reading of the claims that requires a prior art reference to explicitly disclose the limitation "absent an immediately preceding loading dose regimen" where the reference already clearly discloses the "daily dose" as claimed and is silent regarding a loading dose. *See New Hampshire v. Maine*, 532 U.S. 742, 750-51 (2001) (providing factors for judicial estoppel); *Minn. Mining & Mfg. Co. v. Chemque, Inc*., 303 F.3d 1294, 1303 (Fed. Cir. 2002); *In re Coastal Plains, Inc*., 179 F.3d 197, 205 (5th Cir. 1999) (judicial estoppel protects "the integrity of the judicial process, by preventing

[6] References to the knowledge or understanding of a POSA or a POSA's interpretation or understanding of a prior art reference are as of the earliest possible priority date, June 27, 2006, unless specifically stated otherwise.

[7] The Apotex IPR is part of the intrinsic evidence of the '405 patent. *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360-1362 (Fed. Cir. 2017).

parties from playing fast and loose with the courts to suit the exigencies of self interest." (internal quotation marks, alterations, and citation omitted)).

3. Claim Construction

While no claim terms require construction,[8] the preambles of independent claims 1, 3, and 5 must be understood as non-limiting statements of purpose and intended result. The claims' preambles merely state the intended result of administering 0.5 mg daily of fingolimod, and do not invoke either an efficacy element or a requirement that the fingolimod regimen be administered with the purpose of treating RRMS. Further, none of the preambles result in any manipulative difference in the steps of the regimen. Whether one wants to treat RRMS, slow the progression of RRMS, or reduce relapses in RRMS, the method to achieve that purpose—as recited in the body of each claim—is identical.

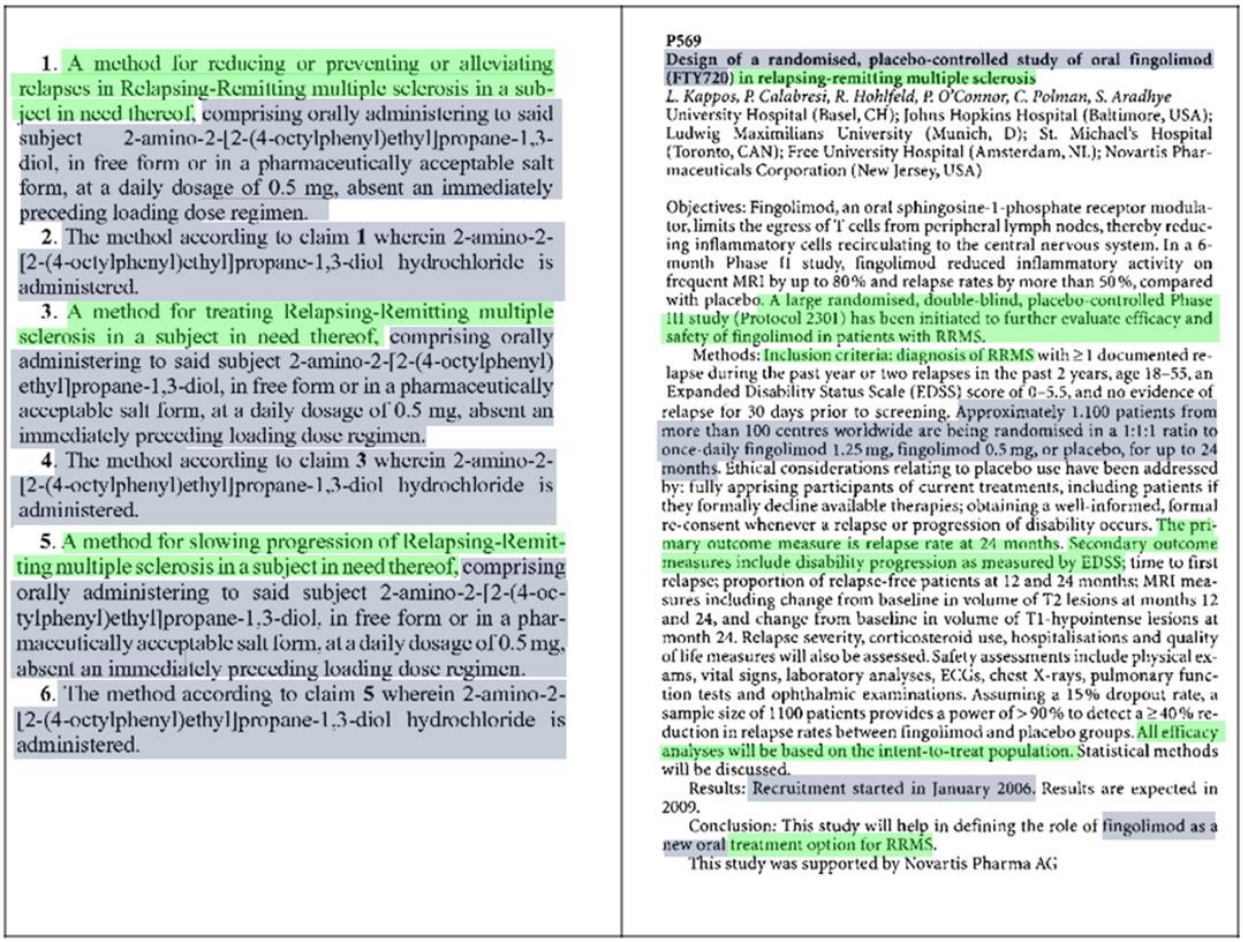
4. Kappos 2006 Anticipated the Claims of the '405 Patent

A patent claim is invalid as anticipated if "the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b) (pre-AIA). Here, every element of the claims of the '405 patent is found, either expressly or inherently, in Kappos 2006, rendering each claim anticipated regardless of the outcome of claim construction. P. Hoffman ¶¶ 76-91; *see also Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.") (collecting cases). A court may afford greater weight to a prior art

[8] Novartis asserts that the term "daily dosage of 0.5 mg" requires construction, and proposes that the term means "[t]he amount of fingolimod administered per day over the course of a multi-day treatment." Defendants assert that the phrase does not require construction. Regardless, the claims are invalid even if Novartis is correct because the prior art cited here disclosed multi-day treatments with 0.5 mg fingolimod.

reference not considered by the PTO. *See Sciele Pharma Inc. v. Lupin Ltd.*, 684 F.3d 1253, 1260 (Fed. Cir. 2012). Here, Kappos 2006 was not considered by the PTO in any proceeding.

Kappos 2006 expressly discloses a Phase III clinical study comprising oral administration of daily doses of 0.5 mg of fingolimod to RRMS patients, absent an immediately preceding loading dose. P. Hoffman ¶¶ 80-82; Kappos 2006 at 143-44. These are the very same steps that comprise the methods of claims 1-6. P. Hoffman ¶ 89; Ex. 62 (Lublin Dep.) at 114:19-115:16. Nothing more is required to anticipate the asserted claims. *See* P. Hoffman ¶¶ 76-91; *see also Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1381 (Fed. Cir. 2003) ("An anticipatory reference need only enable subject matter that falls within the scope of the claims at issue, nothing more."); *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378 (Fed. Cir. 2001) (a reference disclosing performance of "all of the claimed steps at dosage levels that anticipate those in the claims" invalidates the claims even if the reference did not report on the "anticancer effects" recited in the preambles); *In re Montgomery*, 677 F.3d 1375, 1382 (Fed. Cir. 2012) (prior art inherently anticipates claimed method as long as it discloses in an enabling manner the administration step). The figure below demonstrates the anticipating disclosures of Kappos 2006:



1. A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

2. The method according to claim **1** wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

3. A method for treating Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl) ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

4. The method according to claim **3** wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

5. A method for slowing progression of Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

6. The method according to claim **5** wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

P569

Design of a randomised, placebo-controlled study of oral fingolimod (FTY720) in relapsing-remitting multiple sclerosis

L. Kappos, P. Calabresi, R. Hohlfeld, P. O'Connor, C. Polman, S. Aradhye
University Hospital (Basel, CH); Johns Hopkins Hospital (Baltimore, USA); Ludwig Maximilians University (Munich, D); St. Michael's Hospital (Toronto, CAN); Free University Hospital (Amsterdam, NL); Novartis Pharmaceuticals Corporation (New Jersey, USA)

Objectives: Fingolimod, an oral sphingosine-1-phosphate receptor modulator, limits the egress of T cells from peripheral lymph nodes, thereby reducing inflammatory cells recirculating to the central nervous system. In a 6-month Phase II study, fingolimod reduced inflammatory activity on frequent MRI by up to 80% and relapse rates by more than 50%, compared with placebo. A large randomised, double-blind, placebo-controlled Phase III study (Protocol 2301) has been initiated to further evaluate efficacy and safety of fingolimod in patients with RRMS.

Methods: Inclusion criteria: diagnosis of RRMS with ≥1 documented relapse during the past year or two relapses in the past 2 years, age 18–55, an Expanded Disability Status Scale (EDSS) score of 0–5.5, and no evidence of relapse for 30 days prior to screening. Approximately 1,100 patients from more than 100 centres worldwide are being randomised in a 1:1:1 ratio to once-daily fingolimod 1.25 mg, fingolimod 0.5 mg, or placebo, for up to 24 months. Ethical considerations relating to placebo use have been addressed by: fully apprising participants of current treatments, including patients if they formally decline available therapies; obtaining a well-informed, formal re-consent whenever a relapse or progression of disability occurs. The primary outcome measure is relapse rate at 24 months. Secondary outcome measures include disability progression as measured by EDSS; time to first relapse; proportion of relapse-free patients at 12 and 24 months; MRI measures including change from baseline in volume of T2 lesions at months 12 and 24, and change from baseline in volume of T1-hypointense lesions at month 24. Relapse severity, corticosteroid use, hospitalisations and quality of life measures will also be assessed. Safety assessments include physical exams, vital signs, laboratory analyses, ECGs, chest X-rays, pulmonary function tests and ophthalmic examinations. Assuming a 15% dropout rate, a sample size of 1100 patients provides a power of >90% to detect a ≥40% reduction in relapse rates between fingolimod and placebo groups. All efficacy analyses will be based on the intent-to-treat population. Statistical methods will be discussed.

Results: Recruitment started in January 2006. Results are expected in 2009.

Conclusion: This study will help in defining the role of fingolimod as a new oral treatment option for RRMS.

This study was supported by Novartis Pharma AG

'405 patent at 12:49-13:9 (claims 1-6); Ex. 2 at DEFSPRIORART-000172-73.

Novartis argues that Kappos 2006 cannot anticipate because the preambles of the claims require that the method be performed for the purposes of treating RRMS, alleviating, preventing, or reducing relapses in RRMS, or slowing progression of RRMS. Br. at 15. This argument ignores the explicit disclosures in Kappos 2006 that the 0.5 mg daily doses of fingolimod were administered with the specific intent of treating RRMS with defined clinical endpoints of "relapse rate at 24 months" and "disability progression." Ex. 2 at DEFSPRIORART-000173; P. Hoffman at ¶ 83; Ex. 62 (Lublin Dep.) at 115:23-116:5. By disclosing these intended purposes of treatment with fingolimod, Kappos 2006 anticipated. *See Iovate Health Scis., Inc. v. Bio-Engineered Supplements & Nutrition Inc.*, 586 F.3d 1376, 1382 (Fed. Cir. 2009) (finding that

even if a claim's preamble was construed to require effectiveness of the claimed method, an "ad's disclosure of a certain composition taken for a certain purpose suffice[d] for the purpose of anticipation" (citing *Bristol-Myers*, 246 F.3d at 1378)).

Should, as Novartis suggests, the Court find the preambles of the asserted claims require proof of actual efficacy—*i.e.* treating RRMS, reducing relapses in RRMS, and slowing the progression of RRMS (Br. at 15)—Kappos 2006 still anticipates the claimed methods. *See* Ex. 62 (Lublin Dep.) at 116:7-13 (Q. "So between Claim 1 and Kappos 2006, what is required of Claim 1 [sic.]—that is not already stated in Kappos 2006?"; A. "Evidence of succeeding in the testing."). It is undisputed that if the method steps described in both Kappos 2006 and the claims were performed before or after the '405 patent was sought, the results would be the same: RRMS would be treated, relapses would be reduced, and progression of RRMS would be slowed. P. Hoffman at ¶ 88; Ex. 62 (Lublin Dep.) at 105:18-106:14, 106:18-107:16, 108:10-23.

Significantly, in light of the results in humans reported in Kappos 2006, a POSA would not have gone back to refer to preclinical animal testing, such as EAE results, for information on fingolimod dosing. In other words, since Kappos 2006 reports results in actual human RRMS patients, a POSA would have had no reason to doubt fingolimod's efficacy in humans based on preclinical animal data. P. Hoffman ¶ 87. Thus, the dosing regimen taught by Kappos 2006 inherently results in actual efficacy.

The conclusion of inherency accords with Federal Circuit authority on method of treatment claims. *See Perricone v. Medicis Pharm. Corp*., 432 F.3d 1368, 1377 (Fed. Cir. 2005) ("[A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." (citations omitted)); *see also Bristol-Myers*, 246 F.3d at 1376 ("Newly discovered results of known processes directed to the same

purpose are not patentable because such results are inherent."); *Montgomery*, 677 F.3d at 1381 ("[W]e agree with the Board that ***even if the claim includes an efficacy requirement***, efficacy is inherent in carrying out the claim steps." (emphasis added)).

In the prior-art reference described in *Montgomery*, as in Kappos 2006, the disclosed clinical trial had been started but not completed at the time of the reference's publication. *See* 677 F.3d at 1378. Montgomery argued that the lack of complete performance rendered the reference "a proposal for future research that was not enabled" and that the claim preambles required proof of actual efficacy even though the patent itself, like the '405 patent, did not include results of any clinical trials. *See id*. at 1379-80, 1383; *see also* Br. at 15-18 (Novartis offering these same arguments). The court rejected Montgomery's assertions, finding that the methods of treatment described in the reference and claimed in the patent were identical and inevitably would have resulted in the effects claimed in the preambles, resulting in the reference being an anticipating disclosure. *See Montgomery*, 677 F.3d at 1381-83. The same result follows here with Kappos 2006 and claims 1-6.

Novartis also suggests that other references—including confidential documents not available to the POSA—may negate anticipation because they could render Kappos 2006 not enabled, by providing additional information that might suggest the disclosed methods would be ineffective or by disclosing the possibility that the FREEDOMS trial included a loading dose regimen. Br. at 7-8. Anticipation, however, focuses on the disclosure of a single reference regardless of what else might be known publicly or privately about the subject matter, contradictory or not. *See, e.g., Celeritas Techs., Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998) (the question of "whether a reference 'teaches away' from the invention is inapplicable to an anticipation analysis"). And a POSA, of course, could not have

considered confidential information that was unavailable to the public when evaluating the teachings of Kappos 2006 when the application for the '405 patent was filed. P. Hoffman ¶ 86; Ex. 62 (Lublin Dep.) at 120:11-20, 121:4-8, 139:18-141:7, 149:16-24, 150:13-23, 178:7-179:5.

Regardless, binding authority establishes that in the context of a claimed method for treating a disease, a prior art reference need not disclose proof of efficacy to anticipate the claim. *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325–26 (Fed. Cir. 2005). If one of ordinary skill in the art would know how to "make and use" the invention based on the reference's disclosure, it is enabling under § 102. *In re Gleave*, 560 F.3d 1331, 1335 (Fed. Cir. 2009). For method claims, a reference is enabling if it shows a POSA how to use—in other words, practice or carry out—the method. *Id.*; *see also Montgomery*, 677 F.3d at 1382 ("We stated that anticipation 'requires only an enabling disclosure,' not 'actual creation or reduction to practice,' so that 'actual administration of loratadine to patients [in the prior art] is irrelevant — the prior art patent inherently anticipated as long as it 'disclose[d] in an enabling manner the administration of loratadine to patients.'" (alterations in original) (quoting *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1380 (Fed. Cir. 2003)). The experts agree that a POSA could have practiced the method of administering oral daily doses of fingolimod, absent an immediately preceding loading dose, based on the teachings of Kappos 2006 before the '405 patent application was filed. P. Hoffman at ¶¶ 80, 89-90; Ex. 62 (Lublin Dep.) 101:25-9, 104:7-106:2; Lublin ¶ 121 ("I don't know why anyone would think about [an immediately preceding loading dose] based on what's written there" when a reference teaches a daily dosage of 0.5 mg of fingolimod without explicitly disclosing a loading dose regimen. (quoting Trenchard Ex. 18 at 228:5-18)).

B. If Not Anticipated, the '405 Patent Is Invalid for Failure to Comply with Section 112.

1. Legal Standards

A patent specification must provide sufficient information to allow a person of ordinary skill in the art to make and use the invention claimed. 35 U.S.C. § 112, ¶ 1 (pre-AIA) states that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A patent's written description "must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (alteration in original) (citation omitted). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* The "hallmark of written description is disclosure." *Id.* When a negative claim limitation is at issue (as it is here), the specification must "describe[] a reason to exclude the relevant limitation." *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1355 (Fed. Cir. 2015) (quoting *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012)).

A patentee cannot rely solely on the knowledge of someone skilled in the art to furnish the information to make or use the invention where the patent itself fails to enable the claims. *See Genentech*, 108 F.3d at 1366 (stating that the rule that a specification need not disclose what is well known in the art is "merely a rule of supplementation, not a substitute for a basic enabling disclosure"). "[T]he enablement inquiry turns on whether the skilled artisan, *after reading the specification*, would be able to make and use the claimed invention without undue

experimentation, based on the ordinary skill in the art." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1310 (Fed. Cir. 2015) (emphasis added).

The enablement requirement incorporates the requirement of 35 U.S.C. § 101 that the specification disclose "a practical utility of the invention." *In re Cortright*, 165 F.3d 1353, 1356 (Fed. Cir. 1999) (quoting *In re Ziegler*, 992 F.2d 1197, 1200 (Fed. Cir. 1993)).

A patent specification that simply sets forth an unproved hypothesis or research plan cannot satisfy the judicially-created utility/enablement requirement:

> If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis.

Rasmusson, 413 F.3d at 1325; *see also In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir 2005) ("It thus is clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research."); *Hitzeman v. Rutter*, 243 F.3d 1345, 1357 (Fed. Cir. 2001) (holding that policy behind the patent laws is to "promote disclosure of inventions, not of research plans" (citation omitted)). A patent specification that "even read in the light of the knowledge of those skilled in the art, does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis," is insufficient to establish the patentability of a method of treatment claim. *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1327 (Fed. Cir. 2009).

If the Court construes the '405 patent claims to require proof of efficacy, the patent is invalid. The specification lacks any clinical test results to show that 0.5 mg fingolimod is effective in treating RRMS in humans, and a POSA would not have recognized the claimed

method's utility in light of the specification's disclosures. Therefore, the claims of the '405 patent are not properly described or enabled.

2. The '405 Patent Specification.

It is undisputed that the '405 patent contains no human testing data. P. Hoffman ¶¶ 93-96, 101-02; Ex. 62 (Lublin Dep.) at 85:13-16; Ex. 102 (Steinman Dep.) at 93:5-25. Instead, Novartis included summary results from a single preclinical test of fingolimod in a rat model that cannot be directly translated to treatment of RRMS in humans and a prophetic protocol for a clinical investigation in humans that had yet to be completed. '405 patent, at 10:32-11:19; P. Hoffman ¶¶ 96-98.

By the time Novartis sought the '405 patent, fingolimod (chemical name, aka "Compound A") was a known S1P-receptor modulator. P. Hoffman ¶¶ 55-56; Steinman ¶ 38. Novartis described a single study in the specification wherein fingolimod was administered to rats that had been artificially induced with Experimental Autoimmune Encephalomyelitis ("EAE"). '405 patent at 10:32-11:2; P. Hoffman ¶ 74. EAE testing was recognized in the art as a surrogate model for examining certain aspects or symptoms of RRMS. P. Hoffman ¶¶ 97, 105; Ex. 62 (Lublin Dep.) at 67:19-68:15. A POSA, however, would have understood in 2006 that EAE results do not necessarily translate into efficacy in humans. P. Hoffman ¶¶ 96-97, 104-05; Ex. 62 (Lublin Dep.) at 69:8-71:2; Ex. 102 (Steinman Dep.) at 81:2-24.

The '405 patent does not contain any explanation or guidance for converting the dosages of fingolimod administered to rats into pharmaceutically useful doses for administration in humans, especially with RRMS. P. Hoffman ¶¶ 97-98, 105-06; Ex. 62 (Lublin Dep.) at 75:24-76:7, 84:22-85:11. Moreover, a POSA could not take the cursory information from the EAE study as disclosed and deduce an appropriate, let alone effective, dose for treatment of RRMS in a human subject based on the patent specification. P. Hoffman ¶¶ 96-98, 104-06; Ex. 102

(Steinman Dep.) at 84:1-87:2. For example, the specification identifies multiple dosing regimens that "completely inhibit[] the relapse phases" of EAE, but does not identify which, if any, would correlate to a 0.5 mg daily dosage of fingolimod in humans. '405 patent at 10:64-11:2. Novartis's experts attempt to fill in these gaps by relying on extrinsic, and sometimes confidential, analyses irrelevant to a Section 112 determination. P. Hoffman ¶ 98; Ex. 102 (Steinman Dep.) at 84:1-87:2, 90:1-91:16.

The "Investigational Clinical Study" in the specification at first appears to describe actual human testing, but there is no dispute that the "study" comprises a hypothetical research plan. P. Hoffman ¶¶ 93-94, 101-02; Ex. 62 (Lublin Dep.) at 38:24-40:3, 85:13-16; Ex. 102 (Steinman Dep.) at 50:24-54:23. Although the specification indicates that Novartis imagined administering fingolimod in specific daily dosages as a treatment for RRMS, the specification is devoid of any data or test results showing the efficacy of 0.5 mg daily-oral fingolimod for "reducing or preventing or alleviating relapses," "treating," or "slowing progression" of RRMS. In fact, the clinical study description only identifies "[m]ain variables for evaluation: [s]afety (adverse events), standard serum biochemistry and hematology, magnetic resonance imaging (MRI)," without any indication of what adverse events to measure or what to look for in MRI results. '405 patent, at 11:17-19. The inclusion of broad dosing ranges in the paragraph following the proposed clinical study without stating a preference for any of the three dosages to be studied serves to confirm that Novartis did not know what results the proposed study would obtain. '405 patent, at 11:20-38; P. Hoffman ¶¶ 95, 103.

The '405 patent specification contains no mention of a loading dose, or lack thereof.

3. The '405 Patent Lacks an Adequate Written Description of the Invention.

The claims of the '405 patent are directed to methods of treating RRMS by orally administering fingolimod (in free form or as in the hydrochloride salt form) at a daily dosage of

0.5 mg, absent an immediately preceding loading dose regimen. The '405 patent specification shows that Novartis had yet to establish the efficacy of 0.5 mg daily doses of fingolimod for RRMS treatment. Likewise, the specification and originally filed claims in GB0612721.1 are silent on administering loading doses. Ex. 62 (Lublin Dep.) at 132:21-137:10 (discussing Ex. 104).

Kappos 2006 discloses all of the elements of asserted claims 1-6 of the '405 patent in connection with a more detailed description of an actual fingolimod clinical trial. *See* Section I.A.4, above. If Kappos 2006 does not anticipate those claims because the Phase III clinical trial had not been completed, then the '405 patent specification provides even less disclosure of efficacy such that the Court cannot find the inventors possessed the claimed method of using a 0.5 mg daily dose. P. Hoffman ¶¶ 100-09.

Both the '405 patent specification and Kappos 2006 make no mention of loading dose regimens for fingolimod. Novartis's experts opine that the "Investigational Clinical Study" discloses a "complete dosing regimen" that precludes administration of an immediately preceding loading dose, but offer inconsistent testimony as to whether the dosing regimen of Kappos 2006 would permit a loading dose regimen. *See, e.g.*, Lublin at ¶¶ 120-25, 128; Ex. 62 (Lublin Dep.) at 125:8-130:4. Novartis cannot have it both ways – if Kappos does not disclose the absence of a loading dose, neither does the patent; if Kappos 2006 could include a loading dose regimen, so could the patent's clinical investigation. Should the Court find that silence does not equate to absence, Novartis did not describe any method supporting possession of the claims. P. Hoffman ¶¶ 107-09.

Thus, if Kappos 2006 does not anticipate claims 1-6, then those claims lack written description under 35 U.S.C. § 112 and are invalid. P. Hoffman ¶¶ 100-110.

4. The '405 Patent Lacks an Enabling Description of the Invention and Its Utility.

The experts agree the '405 patent discloses a research plan only for testing fingolimod in humans. P. Hoffman ¶¶ 93-94; Ex. 102 (Steinman Dep.) at 56:24-58:24. At best, the only evidence of utility in the patent arises in the context of the rat EAE study.

Novartis and its experts cannot point to any portion of the specification that contains actual information supporting the claimed utility in human patients. *See, e.g.*, Br. at 23. Noticeably absent from any of Novartis's filings is any citation to where the intrinsic record shows that "doses 58% lower than any before effective" in EAE could work or where a POSA could "expressly correlate[] EAE results with doses as low as 0.5 in humans." *Id.*; *see also* P. Hoffman ¶¶ 96-98; Ex. 62 (Lublin Dep.) at 69:8-71:2; Ex. 102 (Steinman Dep.) at 81:2-24. In other words, Novartis relies solely on "prognosticated" expert testimony devising a *post hoc* rationalization for how the disclosed EAE results could justify the claimed dosing regimens and therapeutic efficacy. *Id.*

Kappos 2006 plainly discloses an actual Phase II human study that demonstrated efficacy and an ongoing Phase III clinical trial using a 0.5 mg daily dose of fingolimod to treat human patients suffering from RRMS. The EAE study, on the other hand, simply provides a pathway for advancing fingolimod into human studies that may or may not be predictive of effectively treating RRMS. P. Hoffman ¶¶ 96-98; Ex. 62 (Lublin Dep.) at 70:15-71:2. Kappos 2006 provides human data that is absent from the '405 patent. Should the Court agree with Novartis's experts that Kappos 2006 would not meet the requirements of the claims for lacking proof of efficacy or dosing fingolimod without a loading dose, neither does any information described in the '405 patent specification. P. Hoffman ¶¶ 92, 99. Novartis should not be permitted to have its cake and eat it too.

For at least these reasons, the '405 patent claims are invalid for lack of enablement and utility under 35 U.S.C. §§ 112/101.

II. NOVARTIS CANNOT SHOW SUBSTANTIAL AND IMMEDIATE IRREPARABLE HARM

Novartis must also "make 'a clear showing' that it is at risk of irreparable harm, which entails showing 'a likelihood of substantial and immediate irreparable injury.'" *Apple*, 678 F.3d at 1325 (citations omitted).[9] "The key word in this consideration is *irreparable*." *Sampson v. Murray*, 415 U.S. 61, 90 (1974) (emphasis added) (citation omitted). A clear showing of irreparable harm is indispensable. Without it, a preliminary injunction cannot issue irrespective of a movant's showing on the other factors. *Amazon.com*, 239 F.3d at 1350. Generic competition will not cause Novartis *irreparable* harm.

The mere loss of money can be compensated by a damages award, and thus is not irreparable harm. *Sampson*, 415 U.S. at 90; *Teva*, 572 U.S. at 1301. The Federal Circuit has rejected the argument that "the sharp economic consequences of open competition from generic drugs establish the inadequacy of monetary damages and irreparable harm." *Abbott Labs., Inc. v. Andrx Pharm., Inc.*, 452 F.3d 1331, 1347 (Fed. Cir. 2006); *see also id.* at 1348 ("we do not doubt that generic competition will impact [plaintiff's] sales …, but that alone does not establish that [its] harm will be irreparable"). In the context of imminent generic competition into a multi-billion-dollar branded drug market, the Chief Justice has similarly held that injunctive relief is "unwarranted" where patent damages are available. *Teva*, 572 U.S. at 1302.

A. Novartis's Delay in Filing Suit Defeats Its Claim of Irreparable Harm.

Novartis's delay in bringing suit strongly weighs against its claim of irreparable harm. Defendants filed their ANDAs starting in 2014 and began providing Novartis notice of the

[9] Although in the past courts sometimes applied a presumption of irreparable harm on a showing of likelihood of success on a patent infringement claim, that presumption has been abolished. *Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1149 (Fed. Cir. 2011).

Defendants' Paragraph IV certifications related to the '405 patent after it issued in late 2015. *See* Compl. ¶¶ 7, 18, 29, 40, 50, 60, 71, 82, 92, 100, 110, 122, 134, 144, 158, 168, 177, 187, 198, and 209. However, Novartis waited more than *31 months* after the '405 patent issued to bring suit.[10] "[D]elay in seeking a remedy is an important factor bearing on the need for a preliminary injunction," and this 31-month delay casts doubt on Novartis's apparent urgency here. *High Tech Med. Instrumentation, Inc. v. New Image Indus., Inc.*, 49 F.3d 1551, 1557 (Fed. Cir. 1995) (relying in part on an almost 17-month delay to reverse a district court's grant of a preliminary injunction); *see also Chestnut Hill Sound Inc. v. Apple Inc.*, No. 15-261-RGA, 2015 WL 6870037, at *4 (D. Del. Nov. 6, 2015) (finding that an over three-year delay in bringing suit supported denying preliminary injunction request); *Sebela*, 2017 WL 4782807, at *8 (Sebela "had multiple opportunities to assert the '237 patent. Instead, it appears that Sebela chose to wait for a decision on the validity of related patents in the Prior Litigation. Sebela's litigation approach belies the alleged emergent nature of the harm." (citations omitted)); *Neology, Inc. v. Fed. Signal Corp.*, No. 11-672-LPS/MPT, 2012 WL 2308202, at *16-17 (D. Del. June 18, 2012) (recommending denial of preliminary injunction request based in part on delay despite plaintiff's awareness of infringing activity) (recommendation adopted, 2012 WL 3236718).

B. Novartis's Alleged Harms Are Not Irreparable.

Novartis alleges four types of harms it contends are irreparable: price erosion; loss of market share; harm to different products; and harm to goodwill and relationships. None of these alleged harms can withstand scrutiny under the circumstances here.

1. Defendants' Launches Would Not Cause Irreparable Price Erosion.

A generic launch would not cause irreparable price erosion because Novartis has

[10] Novartis has been aware of Gilenya's® loss of exclusivity for years and been developing strategies to prepare for such an event. I. Hofmann ¶¶ 84-91.

numerous business options available to counteract any potential price erosion, and any price erosion ultimately experienced would be quantifiable. I. Hofmann ¶¶ 32-37, 39-53, 92-94. Specifically, Novartis can choose to maintain its historical Gilenya® pricing and support services; lower pricing to compete with generic fingolimod and temporarily eliminate those services; [redacted] or choose a middle ground or any combination of options. *Id*. ¶¶ 33-37, 39-53.

Novartis alleges Gilenya will suffer "[i]rreversible price erosion" because it *might* not be able to raise its prices back to original levels due to Novartis's relationships and contracts with institutional payors, and competitors in the solid oral RRMS market. Br. at 26. Even Novartis does not go so far as to allege it could not return Gilenya to its current pricing structure after withdrawal of a generic product. Regardless, Novartis provides no *evidence* to support its argument, relying on ungrounded assumptions and ignoring unhelpful facts. Bare allegations of price erosion do not show irreparable harm. *Neology*, 2012 WL 2308202, at *29 ("[I]n order to demonstrate irreparable harm the movant must show that its 'price erosion damages are incapable of being quantified, or that [the movant] could not be fully compensated by a monetary award.'" (alteration in original) (citation omitted)). Further, "[s]ales lost to an [allegedly] infringing product cannot irreparably harm a patentee if consumers buy that product for reasons other than the patented feature." *Apple*, 678 F.3d at 1324.

[redacted] Ex. 103 (NPCFINGO005178460-76) at NPCFINGO005178476; I. Hofmann ¶ 35. [redacted]. *See, e.g.*, *Altana Pharma AG v. Teva Pharm. USA, Inc.*, 532 F. Supp. 2d 666, 682-83 n.26 (D.N.J. 2007),

aff'd, 566 F.3d 999 (Fed. Cir. 2009); *ViroPharma Inc. v. Hamburg*, 898 F. Supp. 2d 1, 27 (D.D.C. 2012).

2. Alleged Loss of Market Share Is Not Irreparable Harm.

Although Novartis argues that it will experience irreparable loss of market share for Gilenya® in the event of a generic launch, Novartis can return to 100% market share and recover its market position if it prevails at trial. I. Hofmann ¶¶ 38, 54-62. Novartis also argues it would suffer loss of market share because generic entry might [redacted] Br. at 27-28. These harms are not irreparable. Rather, they are ordinary, quantifiable financial harms, compensable, especially by multiple generics, if Novartis were to prevail in this case; defendants can satisfy any award; and the arguments Novartis makes here would block virtually every generic launch. *See* I. Hofmann ¶¶ 32-62, 92-94.

"[N]either the difficulty of calculating losses in market share, nor speculation that such losses might occur, amount to proof of special circumstances justifying the extraordinary relief of an injunction prior to trial. Indeed, [a] district court's reliance on possible market share loss would apply in every patent case where the patentee practices the invention." *Nutrition 21 v. United States*, 930 F.2d 867, 871 (Fed. Cir. 1991) (citation omitted). In weighing preliminary relief in patent cases, "courts have routinely decided that market share and price erosion do not amount to irreparable harm." *King Pharm., Inc. v. Sandoz, Inc.*, No. 08-5974 (GEB-DEA), 2010 WL 1957640, at *5 (D.N.J. May 17, 2010); *Sebela*, 2017 WL 4782807, at *7 ("'Both loss of market share and price erosion are economic harms and are compensable by money damages' even in the 'context of generic competition in the pharmaceutical industry.'" (alteration omitted) (quoting *Novartis Pharm. Corp. v. Teva Pharm. USA, Inc.*, No. 05-1887, 2007 WL 2669338, at *14 (D.N.J. Sept. 6, 2007), *aff'd*, 280 Fed. App'x 996 (Fed. Cir. 2008)); *Abbott Labs.*, 452 F.3d at 1348 ("[W]e do not doubt that generic competition will impact Abbott's sales . . ., but that

alone does not establish that Abbott's harm will be irreparable."). Holding otherwise would "disserve the patent system" by encouraging "a rash of patentee motions for preliminary injunctions filed without full basis in equity." *Ill. Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679, 683 (Fed. Cir. 1990).

Accepting at face value Novartis's argument, that loss of market share is irreparable harm, "would convert the 'extraordinary' relief of a[n] . . . injunction into a standard remedy, available whenever the plaintiff has shown a likelihood of success on the merits." *Eli Lilly & Co. v. Am. Cyanamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996). That is not the law.

3. Alleged Harm to Goodwill or Loss of Formulary Status Is Not Irreparable.

Novartis tries to pass off various other injuries as irreparable harm, such as possible harm to relationships or loss of current formulary position. I. Hofmann ¶¶ 32-37, 63-69. Again, this is not irreparable harm. Novartis's speculative claims about loss of goodwill fail to acknowledge that brand companies such as Novartis routinely face generic competition and maintain their relationships through such events. *Id.* ¶¶ 63-69. Courts have also found that "damages from loss of formulary positions are reasonably calculable" and that a "loss of tier status will translate into sales losses that should be quantifiable." *AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579, 610 (D.N.J. 2009); *Abbott Labs.*, 452 F.3d at 1334, 1347-48; *Sebela*, 2017 WL 4782807, at *8 ("Sebela's complaint about the alleged harm from changed formulary status . . . is 'another way of saying that Sebela will make less money,' which is compensable in money damages."). Further, there is no reason Novartis cannot maintain or regain its formulary status even assuming Defendants launch. I. Hofmann ¶¶ 32-37. And there is no reason Novartis cannot pursue these strategies after Defendants' launches, [redacted] *See generally* Ex. 103 (NPCFINGO005178460-76).

4. Purported Disruption of Unrelated Launches Is Not Irreparable Harm.

Novartis alleges its launch of other drugs could be impacted if Defendants are not enjoined. However, Mayzent (siponimod) and ofatumumab are still anticipated to launch within the next two years, and are still expected to become blockbusters, despite the expected loss of exclusivity for Gilenya. I. Hofmann ¶¶ 70-83; Vellturo ¶ 40. Further, Mayzent is indicated for SPMS *and* RRMS, and more than eighty percent of people with RRMS go on to develop SPMS. I. Hofmann ¶ 71. Speculation regarding unrelated products, even before they are launched, cannot justify the extraordinary remedy of a preliminary injunction. *Connecticut v. Massachusetts*, 282 U.S. 660, 674 (1931) (an injunction "will not be granted against something merely feared as liable to occur at some indefinite time in the future"); *Eli Lilly*, 82 F.3d at 1578 ("If a claim of lost opportunity to conduct research were sufficient to compel a finding of irreparable harm, it is hard to imagine any manufacturer with a research and development program that could not make the same claim and thus be equally entitled to preliminary injunctive relief. Such a rule would convert the 'extraordinary' relief of a preliminary injunction into a standard remedy, available whenever the plaintiff has shown a likelihood of success on the merits."). Indeed, Novartis documents discuss multiple areas of focus and potential success for Mayzent and ofatumumab, none of which purport to rely on Gilenya whether it has lost exclusivity or not. I. Hofmann ¶¶ 70-83.

C. Any Loss Suffered by Novartis Is Easily Calculable.

Finally, Novartis suggests that "calculating retrospective damages would be uncertain due to the MS market's rapidly-evolving competitive landscape, and the central importance of patient support services in that market." Br. at 25 (citing Vellturo ¶¶119-124). This argument lacks merit. I. Hofmann ¶¶ 31-37, 39-40, 92-94. The pharmaceutical market (brand and generic) has been analyzed numerous times by developing and using financial models to calculate

potential damages. When quantifying damages, financial and economic experts routinely address the purported challenges associated with additional market entrants, price erosion, and promotional activity. *See* I. Hofmann ¶¶ 13, 93. These damages calculations have been accepted by courts for years. If competing companies launch, and pricing, market share, units, and sales are identified (as well as other relevant information), damages will be quantifiable. I. Hofmann ¶¶ 31-34, 39, 92-94.

Importantly, regardless of whether one can *estimate* now Novartis's potential losses from generic competition, the Court would certainly be able to hear evidence later to determine the appropriate *measure* of those losses once they occur. Novartis currently has 100% of the Gilenya market. Dr. Vellturo opines that damages may be "difficult to fully quantify," Vellturo ¶ 4, but that position is untenable given the known state of the market now, its sales and share trends, and the ability to measure changes over the time following any generic launch.

Given the extraordinary nature of the remedy, courts do not find irreparable harm where "the patentee has not *clearly established* that monetary damages *could not* suffice." *Abbott Labs.*, 452 F.3d at 1348 (emphasis added). Neither the mere "difficulty of calculating losses in market share, nor speculation that such losses might occur" suffice to establish irreparable harm. *Nutrition 21*, 930 F.2d at 871; *see also Sebela*, 2017 WL 4782807, at *7 (finding calculable damages reparable by money damages even though the "damages might be significant, and the 'complexities and uniqueness of the pharmaceutical industry might make such calculation an arduous task'"). If it prevails at trial, Novartis "will be able to recover damages … for past patent infringement," and thus has not "shown a likelihood of irreparable harm." *Teva*, 572 U.S.

at 1301 (refusing to block at-risk generic launch pending review of patent invalidity finding).[11]

III. THE BALANCE OF EQUITIES AND PUBLIC INTEREST WEIGH AGAINST AN INJUNCTION

Assessing the balance of hardships and whether an injunction would disserve the public interest are "highly factual inquiries." *Apple*, 678 F.3d at 1332. In balancing hardships, a "court must remain free to deny a preliminary injunction, whatever be the showing of likelihood of success, when equity in the light of all the factors so requires." *Ill. Tool Works*, 906 F.2d at 683. Where the patentee's showing of a likelihood of success is not strong, the public interest in protecting patent rights may be "counterbalanced" by the accused infringer's "continuing right to compete" at the preliminary stage of litigation. *Id*. at 684.

An injunction would significantly harm not just Defendants, but patients and payors too. *See* I. Hofmann ¶¶ 95-106. Third-party payors, Medicare, and Medicaid represent the vast majority of annual payments for prescription drugs, and Novartis will have experienced almost a decade of exclusivity and over $10 billion in net sales related to Gilenya® by August 2019 due to the '229 Patent. *Id.* ¶¶ 103-104. Timely marketing of generic alternatives to Gilenya® will therefore contribute to the substantial drug savings available to the public. *Id.* ¶ 103. An injunction would reward Novartis by artificially extending, even further, its ability to charge monopoly prices and to capture the full scope of increased costs, at the expense of the public.

One of the primary reasons Congress passed the Hatch-Waxman Act was to speed the introduction of low-cost generic drugs to market. *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 404-05 (2012). A preliminary injunction will frustrate that congressional purpose, especially now that Novartis has enjoyed nearly nine years of monopoly profits since

[11] While Dr. Vellturo appears to suggest that some defendants might not be able to satisfy a damages claim (Vellturo ¶ 128), Novartis did not make that argument in its brief, thereby waiving this as a basis to support its motion. Defendants reserve the right to file evidence regarding their ability to satisfy a damages claim should Novartis raise this issue in reply.

Gilenya's approval in September 2010. "The public 'has a well-recognized interest in receiving generic competition to brand-name drugs as soon as possible . . . and a delay in the marketing of [the generic] drug could easily be against the public interest in reduced prices.'" *ViroPharma*, 898 F. Supp. 2d at 29 (citation omitted).

CONCLUSION

For the foregoing reasons, the Court should deny Novartis's request for an injunction.

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CERTIFICATE OF SERVICE

I hereby certify that on April 9, 2019, true and correct copies of the foregoing document were caused to be filed with the Clerk of Court via CM/ECF, which will send notification of the filing to counsel of record, and I further certify that true and correct copies of the foregoing document were caused to be served on the following counsel of record as indicated:

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